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**Original Article**

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## Does Atrial-Pacing from Different Intra-Atrial Sites for Atrial Fibrillation Effect Pulmonary Venous Pressure?

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**Introduction:** Coronary sinus (CS) and biatrial pacing have been reported to be more effective than right atrial appendage (RAA) pacing for preventing atrial fibrillation (AF). However, the effects of atrial pacing on hemodynamics are still unknown.

**Methods and Results:** Eleven patients with AF who underwent PV isolation were studied. Two quadripolar electrode catheters were placed in RAA and CS.

After a transseptal approach, a thermodilution catheter was introduced into the left superior pulmonary vein (LSPV). The mean LSPV pressure was directly measured during pacing from the distal site of the CS (CS-d) and RAA, and simultaneous pacing from CS-d and RAA. The P wave duration during pacing from the RAA+CS-d was significantly shorter than that during pacing from the RAA ( $83 \pm 16$  vs.  $121 \pm 18$  ms,  $P < 0.05$ ). No significant difference in LSPV pressure was found among the three pacing configurations (RAA, CS-d, RAA+CS-d pacing;  $16 \pm 7$ ,  $16 \pm 4$ ,  $17 \pm 3$  mmHg, respectively).

**Conclusions:** LSPV pressure was not affected by CS-d, or biatrial pacing. Shortening of the P wave duration by biatrial pacing may contribute to the prevention of AF. The electrophysiological effects of pacing may play a more important role in preventing AF rather than the hemodynamic effects.

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**Key words:** Pulmonary Venous Pressure, Atrial pacing, Atrial fibrillation

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### Introduction

The conventional method of pacing from the right atrial appendage (RAA) or free wall is often the cause of delayed intra-atrial conduction and dis-coordinate left and right atrial mechanical function. Recent research has suggested that dual-site atrial, biatrial pacing (RAA+ coronary sinus-distal (CS-d) pacing) and single site inter-atrial septum pacing can prevent the recurrence of drug-refractory AF.<sup>1–3)</sup>

Also, it has been noted that simultaneous biatrial pacing prevented AF due to the prolonging of the atrial effective refractory period (AERP) and shortening of the intra-atrial conduction time.<sup>4)</sup> However, the effects of atrial pacing on hemodynamics are not well known.

The pulmonary veins (PVs) are the major sites of the ectopic foci for initiating atrial fibrillation (AF), trigger and maintenance.<sup>5–8)</sup> An increase in intra-atrial pressure related to the initiation of AF using

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a stretch-related mechanism has been reported.<sup>9)</sup> Therefore, this study was conducted to investigate how atrial-pacing from the different intra-atrial sites for atrial fibrillation effect pulmonary hemodynamics.

Measurement of PV pressure was done using Swan-Gantz catheter during sinus rhythm, pacing from RAA and CS-d, and simultaneous pacing from RAA and CS-d (biatrial pacing).

## Methods

### Study Subjects

The subjects in this study consisted of 11 patients (8 male, 3 female, mean age  $59 \pm 10$  years) with drug-refractory AF who had not undergone PV isolation. Paroxysmal AF was defined as AF terminating spontaneously within 24 hours, and persistent AF as AF lasting more than 24 hours. Paroxysmal AF was present in 8 patients (73%) and 3 patients (27%) had persistent AF. The mean morbidity duration of AF was  $21 \pm 21$  months for paroxysmal AF and  $79 \pm 59$  months for persistent AF. A mean of two antiarrhythmic drugs were ineffective in preventing recurrence of AF or restoring sinus rhythm before the ablation procedure. Of these 11 patients, 1 had hypertrophic cardiomyopathy, 10 had no structural heart disease, and 2 had a history of hypertension. Echocardiography demonstrated a mean left ventricular ejection fraction of  $63 \pm 13\%$  (range: 44 to 82%), and mean left atrial diameter of  $41 \pm 7$  mm (range: 32 to 51 mm). (Table 1)

### Measuring PV pressure and Electrophysiological Study

The present study was approved by the Ethics Committee of Fukuoka University Hospital. The electrophysiological study was done in the fasting state after written informed consent was obtained. Antiarrhythmic drugs were discontinued 5 half-lives before the study. Two 5-French quadripolar electrode catheters (Daig Corp., USA) were positioned in the RAA and close to the His bundle area through the left femoral vein. A 10-pole electrode catheter (Daig Corp., USA) was inserted into the CS through the right internal cervical vein. After transseptal puncture, a 7-French thermolab catheter (Goodtec. Inc., USA) was inserted into the left superior PV (LSPV). 100 IU heparin/kg was given intravenously. Atrial pacing from the RAA, CS-d site, and RAA+CS-d were determined at a basic drive cycle length of 600 ms using a programmed stimulator (SEC-3102, Nihon Kohden, Japan). The distal electrode pairs of RAA and CS catheters

**Table 1** Patient's characteristics

Age	$56 \pm 7$
Male/Female	6/1
History of AF (month)	$55 \pm 50$
Hypertension	0 (0%)
Diabetes mellitus	0 (0%)
CAD	1 (16%)
CM	1 (16%)
MR	0 (0%)
LAd (mm)	$40 \pm 5$
EF (%)	$63 \pm 15$
PV diameter (mm)	$18 \pm 5$

MR: mitral regurgitation, CAD: coronary artery diseases, CM: cardiomyopathy, LAd: left atrial dimension, EF: ejection fraction, PV: pulmonary vein.

were used for bipolar stimulation. The stimulus output had a pulse width of 2 ms and was set at twice the diastolic threshold. Particular care was taken to ensure continuous capture of atrial tissue when threshold values were determined.

LSPV pressure and P wave duration (lead II, paper speed 200 mm/s, power setting 32 W) were measured, and intra-cardiac electrogram was recorded during each pacing configuration.

### Statistical Analysis

Continuous variables were analyzed as mean  $\pm$  SD, and differences in continuous variables among the groups were assessed by analysis of variance (ANOVA).  $P < 0.05$  was considered to be statistically significant.

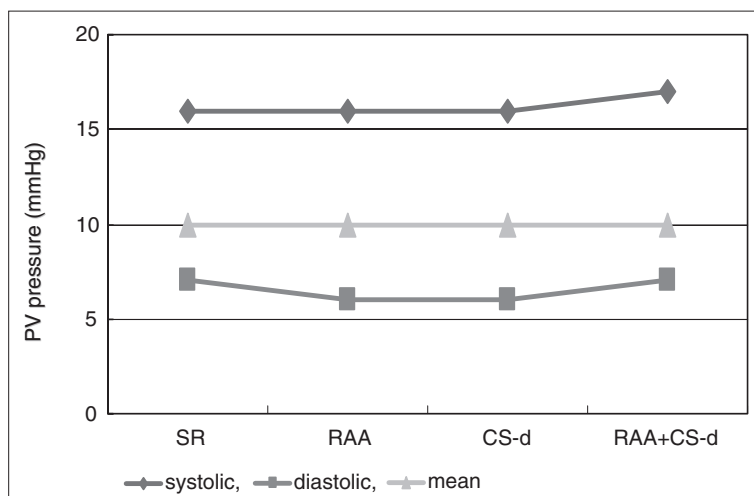
## Results

### PV pressure

For all 11 patients, LSPV pressure was measured during sinus rhythm, RAA, CS-d, and RAA+CS-d pacing. Mean LSPV pressure (systolic/diastolic/mean) was  $16 \pm 5/7 \pm 3/10 \pm 4$  mmHg during sinus rhythm,  $16 \pm 7/6 \pm 4/10 \pm 5$  mmHg during RAA pacing,  $16 \pm 4/6 \pm 3/10 \pm 3$  mmHg during CS-d pacing, and  $17 \pm 3/7 \pm 2/10 \pm 4$  mmHg during RAA+CS-d pacing (Figure 1). No significant differences in the pacing configurations were found in relationship to LSPV pressure.

### P wave duration and intra-cardiac electrogram

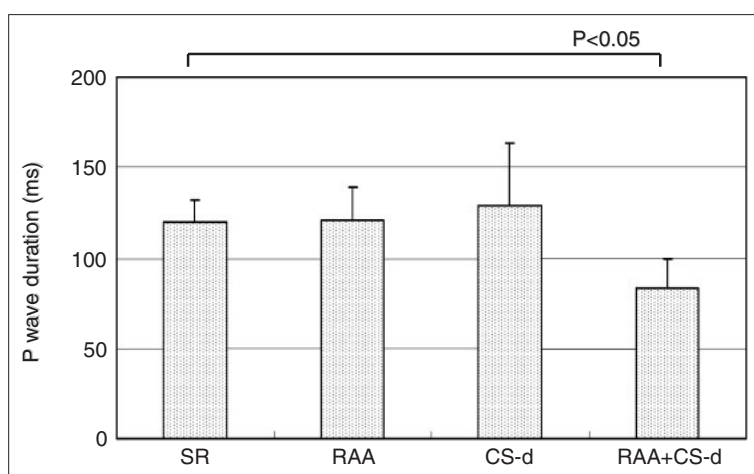
Surface ECG was recorded while in the supine position. P wave onset was defined as the point where the first atrial deflection crosses the isoelectric line, and offset was defined as the point of the return



**Figure 1** Effect of different atrial pacing configurations on the PV pressure.

There were no significant differences in LSPV pressure among the four groups.

SR: sinus rhythm, RAA: right atrial appendage, CS-d: distal coronary sinus



**Figure 2** Effect of different atrial pacing configurations on the P wave duration.

P wave duration was significantly shortened by RAA+CS-d pacing compared with the other pacing modes.

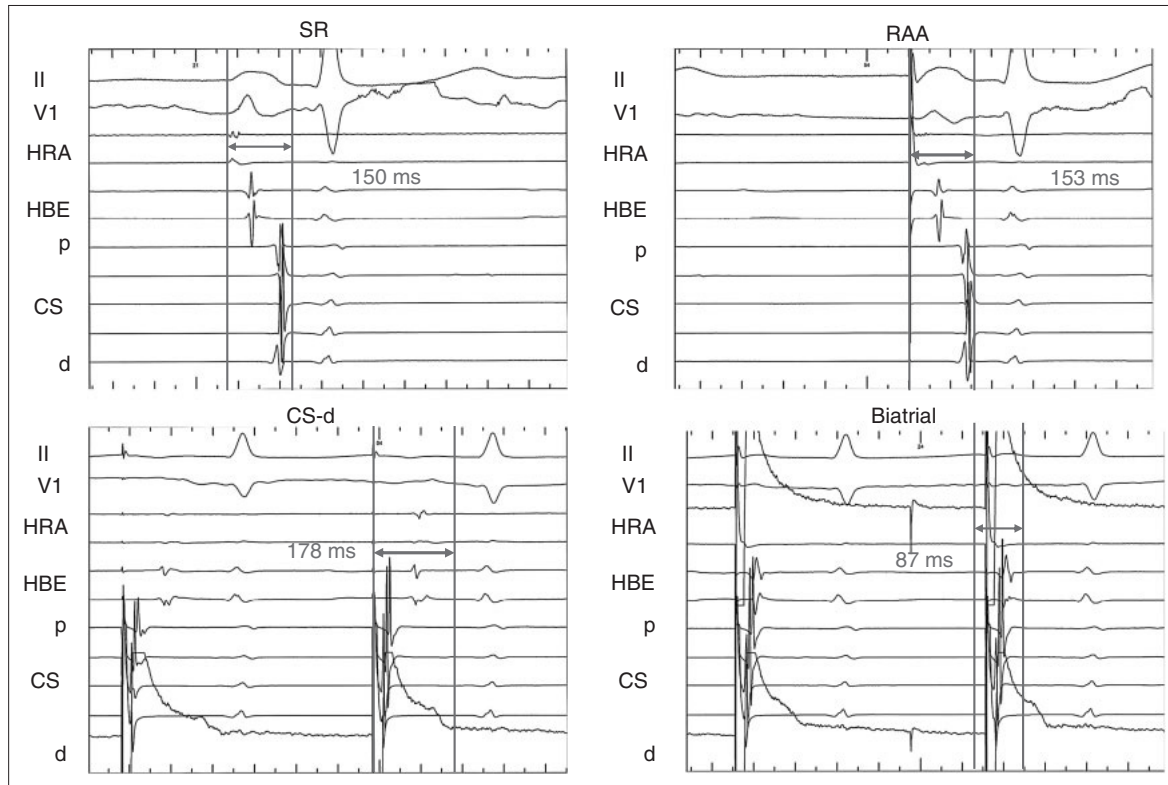
to the atrial signal to baseline. P wave duration on surface ECG lead II (paper speed 200 mm/s, power setting 32 W) was measured during sinus rhythm, RAA, CS-d, and RAA+CS-d pacing. P wave duration was  $120 \pm 12$  ms (range: 104 to 136 ms) during sinus rhythm,  $121 \pm 18$  ms (range: 106 to 149 ms) during RAA pacing,  $129 \pm 34$  ms (range: 94 to 182 ms) during CS-d pacing, and  $83 \pm 16$  ms (range: 74 to 107 ms) during RAA+CS-d pacing. P wave duration was significantly shortened by RAA+CS-d pacing compared with the other pacing configurations (**Figure 2**).

**Figure 3** shows the typical intra-cardiac electrogram during each pacing configuration. The intra-atrial conduction time (interval from each pacing site to the end point of P wave on surface ECG) was measured. These measurements were 150 ms during sinus rhythm, 153 ms during RAA pacing, 178 ms during CS-d pacing, and 87 ms during RAA+CS-d

pacing. Intra-atrial activation ended within 69 ms during RAA+CS-d pacing.

## Discussion

The results of the present study demonstrated no significant difference on LSPV pressure by single-site RAA or CS-d and biatrial pacing, whereas P wave duration was significantly shortened during biatrial pacing compared with single-site RAA and CS-d pacing. Moreover, activation sequence on the intra-cardiac electrogram changed and intra-atrial conduction time was significantly shortened during biatrial pacing. These results suggest that single-site RAA, CS-d, and biatrial pacing do not affect atrial hemodynamics. The previous studies have shown that biatrial pacing from the high right atrium and CS-d prevented AF.<sup>10–12</sup> There is evidence of a beneficial effect on electrophysiological changes



**Figure 3** Intra-cardiac electrogram during each atrial pacing configuration.

Intra-atrial conduction (interval from each pacing sites to the end of P wave on surface ECG) was significantly shortened during biatrial pacing compared with other pacing configurations.

with dual site pacing playing an antifibrillatory role.<sup>13)</sup> In contrast, there was less evidence of hemodynamic change.

The Doppler flow signal across the mitral valve or alterations in the cardiac peptides, atrial natriuretic peptide (ANP) and B-type atrial natriuretic peptide (BNP) are well established indices of cardiac function.<sup>14,15)</sup> Levy et al. investigated the role of a hemodynamic mechanism in biatrial pacing by comparing changes in mitral Doppler flow, ANP and BNP levels during sinus rhythm and right atrial pacing. They suggested that atrioventricular timing sequence and other Doppler hemodynamic parameters or cardiac peptide levels do not change and P-R intervals on the surface ECG are shortened by biatrial pacing. Thus, biatrial pacing does not effect hemodynamic change that could account for any antifibrillatory properties.<sup>16)</sup>

A recent study demonstrated that AF was initiated from PVs based on a stretch-related mechanism due to an increase in atrial pressure.<sup>9)</sup> Moreover, patients with AF had larger PVs, left atrial areas and PV ostial diameters than normal controls on computed tomography/magnetic resonance (CT/MR) slices.<sup>9,18)</sup> Kalifa et al. suggested that an increase

in intra-atrial pressure related to rise of rate and organization of waves origin from the LSPV was associated with atrial stretch.<sup>9)</sup> To assess whether atrial pacing from the different intraatrial sites for AF effect PV pressure in the present study we evaluated the effect of pacing from three different atrial sites on PV pressure in patients with AF. However, these atrial pacing configurations, including biatrial pacing, did not influence PV pressure. The factors related to the prevention of AF must result from other mechanisms. Atrial inhomogeneous conduction and dispersion of AERP play an important role in the maintenance of AF. P wave duration depends on intraatrial conduction delay. Patients with AF have been reported to have P wave duration significantly longer than that of normal controls, and atrial conduction delay is a factor in atrial vulnerability.<sup>17)</sup> Biatrial pacing simultaneously and quickly stimulates both atria, therefore, the activation of all atria finish quickly.

The beneficial effect of biatrial pacing was thought to be mainly due to the shortening of atrial conduction, not due to the improvement of hemodynamics. This could be responsible for prevention of AF. This study suggests that biatrial pacing has the

potential to become useful for the prevention of AF. However, further studies are needed to more fully test the potential.

## Conclusions

Neither CS-d nor biatrial pacing affected LSPV pressure. Shortening of P wave duration by biatrial pacing may contribute to the prevention of AF. The electrophysiological effect of pacing may play a more important role than the hemodynamic effects in preventing AF.

## Limitations of the Study

There are some limitations in our study. We analyzed only 11 patients and AF in isolation. We measured data for only 1 PV in this study and did not observe the effect on other PVs simultaneously.

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